VIA MEDICA

CASE REPORT

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2-year follow-up of lung transplantation as a treatment of hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease)

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Abstract

Hemorrhagic telangiectasia (HHT) is a disease of initially mild course - manifesting with recurrent nosebleeds and increased fatigue. Nevertheless, its progression can deteriorate patient's health. Solid organ transplantation becomes the only therapeutic option to save a life. The case report describes a 19-year-old female patient who was diagnosed with HHT and qualified for lung transplantation. She met the Curacao criteria for HHT (¾). Her health deteriorated significantly to the point of the referral to Department of Cardiac, Vascular and Endovascular Surgery and Transplantology in Silesian Center for Heart Diseases. Due to her condition, she was qualified for lung transplantation as one diagnosed with pulmonary arteriovenous malformations and then transplanted at the age of 17. A direct postoperative period was complicated by HSV2 infection of the wound. 18 months after the procedure, the patient underwent acute cholangitis. The presence of portal and systemic fistulas was noted and the final diagnosis of HHT was made. Despite the fact that proper diagnosis was made posttransplant, it was a good treatment. The patient is currently 2 years after the lung transplantation and feels good.

Lung transplantation is a viable therapeutic option for patients with HHT as there are reports of other patients who have benefited from lung transplantation after other therapeutic options were exhausted.

Key words: lung transplantation, hereditary hemorrhagic telangiectasia, transplantation, arteriovenous malformation

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Introduction

Osler-Rendu-Weber syndrome also known as hereditary hemorrhagic telangiectasia (HHT) is an autosomal-dominant disease that affects 1 in 5,000–8,000 people [1]. Its presentation patterns are highly variable. Some of the symptoms such as epistaxis could manifest before school age [2]. Pulmonary arteriovenous malformations (PAVM) are estimated to be present among 30–50% of patients with HHT. The prevalence of dyspnea among those patients reaches 35% [3]. Abnormal vascular structures can be also present in the liver [1]. Its symptomatic involvement includes high-output heart failure, portal hypertension, and biliary disease [4]. Therapeutic options for HHT patients include embolization and segmental or lobar resections of the lungs [5]. Sporadic PAVM can be treated by transcatheter embolotherapy with Amplatz vascular plugs or coils. This safe method provides great radiological and functional improvement of the patient [6]. However, subjects with HHT and PAVMs face higher risk of embolic complication [7]. Solid organ transplantation, especially lung transplantation can be a viable therapeutic option for patients with HHT and PAVMs [5, 8, 9]. Not only it improves the hypoxemia, but it also has a positive effect on the cerebral arteriovenous malformations [8].

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Case presentation: The case report describes a female patient whose first symptoms were observed when she was few years old. Back then, she reported increased fatigue, post-workout fainting and temporary dry, tiring cough. At the beginning she was diagnosed with allergy and asthma. Despite the treatment, her condition deteriorated. She presented following symptoms: increased fatigue and central and peripheral cyanosis. Full blood count revealed polycythemia. Arterial blood gas test showed hypoxemia with hypercapnia. Fainting after physical exercise persisted. At the age of 14, the patient underwent computed tomography of the chest, which revealed inflammatory changes to be differentiated with chronic interstitial lung disease. Additionally, lung scintigraphy was performed when the patient was 15 years old. Lung perfusion scan of 3mCi with 99mcTc displayed intrapulmonary fistulas. Brain -lungs ratio was 11.5% (normal limit is less than 0.4%). The girl was then diagnosed with pulmonary arteriovenous malformations (PAVMs). Due to constant deterioration of her health (saturation of 81%, post-workout desaturations of 46–50%, persistent central cyanosis and necessary oxygen treatment), she was referred to, and subsequently qualified for lung transplantation in Department of Cardiac, Vascular and Endovascular Surgery and Transplantology in Silesian Center for Heart Diseases. At qualification, she required 2 l/min of supplemental oxygen at rest. Abdominal CT angiography did not reveal any abnormalities at that time. She underwent double lung transplantation at the age of 17 after 378 days spent on Lung Transplantation Waiting List. Post-op course was complicated with HSV infection, but the rest of the recovery period remained uneventful. She was treated with ATG as induction of immunosuppression and tacrolimus, encortolon and mycophenolate mofetil as immunosuppressive maintenance treatment. Pulmonary function was satisfactory and stable for the first 2 years after transplantation. Detailed results of 6-minute walk test (6MWT) and spirometry were presented in Table 1. 18 months after lung transplantation the patient was hospitalized due to pain in the right hypochondrium with nausea and stool discoloration. Diagnosis of acute cholangitis was made. Liver enzymes were also elevated (alanine aminotransferase 186 IU/l, aspartate aminotransferase 310 IU/L). CT scans of the liver, MR of the liver and bile ducts and Doppler ultrasound of the portal system were performed, after which suspicion of secondary changes of sclerosing cholangitis in the course of ischemic changes due to portal and systemic fistulas causing perfusion disorders in the liver parenchyma was aroused. The presence of this additional feature made us rethink the original diagnosis, which was changed posttransplant. Entire clinical presentation of the disease (history of multiple arteriovenous fistulas in the lungs and liver, oral telangiectasias and nosebleeds) as well as a positive family history (hemorrhage from first-line relatives) met the current Curacao criteria of the Osler-Weber-Rendu syndrome (HHT) diagnosis. Nowadays, the patient is alive and well. The intensity of changes is not an indication for endoscopic retrograde cholangiopancreatography (ERCP). After the transplantation, recurrent nosebleeds, pallor of the skin, numerous telangiectasia on the oral mucosa and gums are still reported.

Table 1. 6-minute walk test and spirometry results of female patient after lung transplantation

Number of days after transplantation	Distance [m]	Borg Scale	Saturation before test	Saturation after test	FEV_1 acquired [L]	FEV_1 %	FVC acquired [L]	FVC %
75	93.6	3	93	92	0.97	30	1.2	32
100	260.5	2	95	96	1.2	41	1.36	39
131	341	1	98	94	1.35	48	1.46	44
163	378	1	97	97	1.38	49	1.73	52
225	396.9	1	97	96	1.25	44	1.85	55
309	401	1	98	96	1.49	53	2.14	64
376	389.2	1	97	97	1.6	50	2.04	56
526	440.9	1	98	95	1.57	47	2.13	57
596	441	0,5	99	98	1.52	47	2.38	64
719	455.3	1	99	97	1.64	50	2.37	64

Discussion

Even though the proper diagnosis of HHT was made after the transplantation carried out in the female patient, decision to proceed with this therapeutic option was a good choice. It has been 2 years since the lung transplantation was performed. The 19-year-old patient is alive and well. Fukushima *et al.* [8] presented the case of a female patient with HHT who was qualified for bilateral lung transplantation and successfully transplanted at the age of 18 after waiting 4 years for a graft. 38 months after the transplantation, the Japanese patient was able to achieve the result of 575m during 6MWT. The subject described in this case report walked the distance of 455m during the same examination 24 months after lung transplantation. Another case of pediatric lung transplantation in a 4-year-old patient was presented by Misra *et al.* [5]. For 2.5 years after the transplantation the patient did well, but due to severe deterioration of her pulmonary condition, she was retransplanted the following year. After developing Epstein-Barr-virus-associated lymphocytic bronchiolitis that evolved into a polyclonal post-transplant lymphoproliferative disease and proper treatment, the rest of the post-transplant time was uneventful. At last check-up, which was 10 years after first lung transplantation, she reported increased exercise tolerance, with only occasional shortness of breath . The girl described in this case report also presented similar state of pulmonary function as the Borg scale score at her last check-up was 1. It is worth mentioning that both patients (the described in this case and the presented by Misra *et al.* [5]) were treated with tacrolimus and glucocortocosteroids. Both of them reported occasional epistaxis after transplantation. Older patients with HHT can also benefit from lung transplantation, as it has been proved by case report presented by Svetliza *et al.* [9]. A 39-year-old female patient with multiple bilateral atrioventricular fistulas (AVF) secondary to hereditary hemorrhagic telangiectasia (HHT) underwent single right lung transplantation after previous left upper lobectomy. After 2 years and 10 months she is alive and performs normal activities. Her 6-minute walk distance at this time was 500m, similar to the result obtained by the patient described in this case report. The 39-year-old patient described by Svetliza *et al.* [9] obtained 80% of predicted FEV_1 while the female patient described in this case presented with 50% of predicted FEV_1 within similar follow-up time.

To summarize, lung transplantation is a viable treatment among HHT patients with PAVMs. Increased lung function is not the only benefit of such treatment. What it more, the proper diagnosis of HHT is an important element on the way to successful transplantation and patient's well-being.

Conflict of interest

The authors declare no conflict of interest.

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